Synthesis of Novel 3-Hydroxy-6-Methyl-2-(1-Methyl-3-(5-Methylisoxazol-3-Yl)-5-Aryl-2-Thioxo-2,3-Dihydro-1H-Imidazol-4-Yl)-4H-Pyran-4-Ones

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ABSTRACT

A Convenient method for the synthesis of novel imidazole-2-thiones containing allomaltol and isoxazole fragments was presented. This synthesis involves a one-pot multicomponent reaction of allomaltol, arylglyoxals, isoxazole amines followed by *in situ* addition of alkyl or aryl isothiocyanates. The reaction produces initially the key intermediate *viz*., α-amino ketones and imidazoline -2-thiones which were not isolated. The advantages of this protocol involves mild reaction conditions, atom economy and easy work-up procedure, without intervention of tedious chromatographic process.

Keywords: *One-pot synthesis; imidazole-2-thiones with allomaltol and isoxazole fragments; easy work- up; good yield.*

Introduction:

Multi component reaction (MCRs) have been frequently used by synthetic chemists as a facile mean to generate molecular diversity from bifunctional substituents that react sequentially in an intramolecular fashion. Designing such type of multi-component reactions that achieve formation of multiple bonds in a single operation is one of the major challenges in modern organic synthesis. As such processes avoid time consuming, and costly purification processes, as well as protection-deprotection steps, they are more environmentally benign and atom economic. They provide a powerful tool towards the one-pot synthesis of diverse and complex compounds as well as small and drug -like heterocycles[1]. The high atom economy coupled with a minimum number of chemical steps and the absence of complex catalysts are obvious advantages of MCRs [2,3].

The development of new approaches to the synthesis of 1,3,5-hexatriene systems containing an enol fragment is an actual task. A convenient approach to the synthesis of hydroxyl-containing terarylenes is based on the application of the multi-component reactions[4-6]. Various biological applications have been reported for isoxazoles such as

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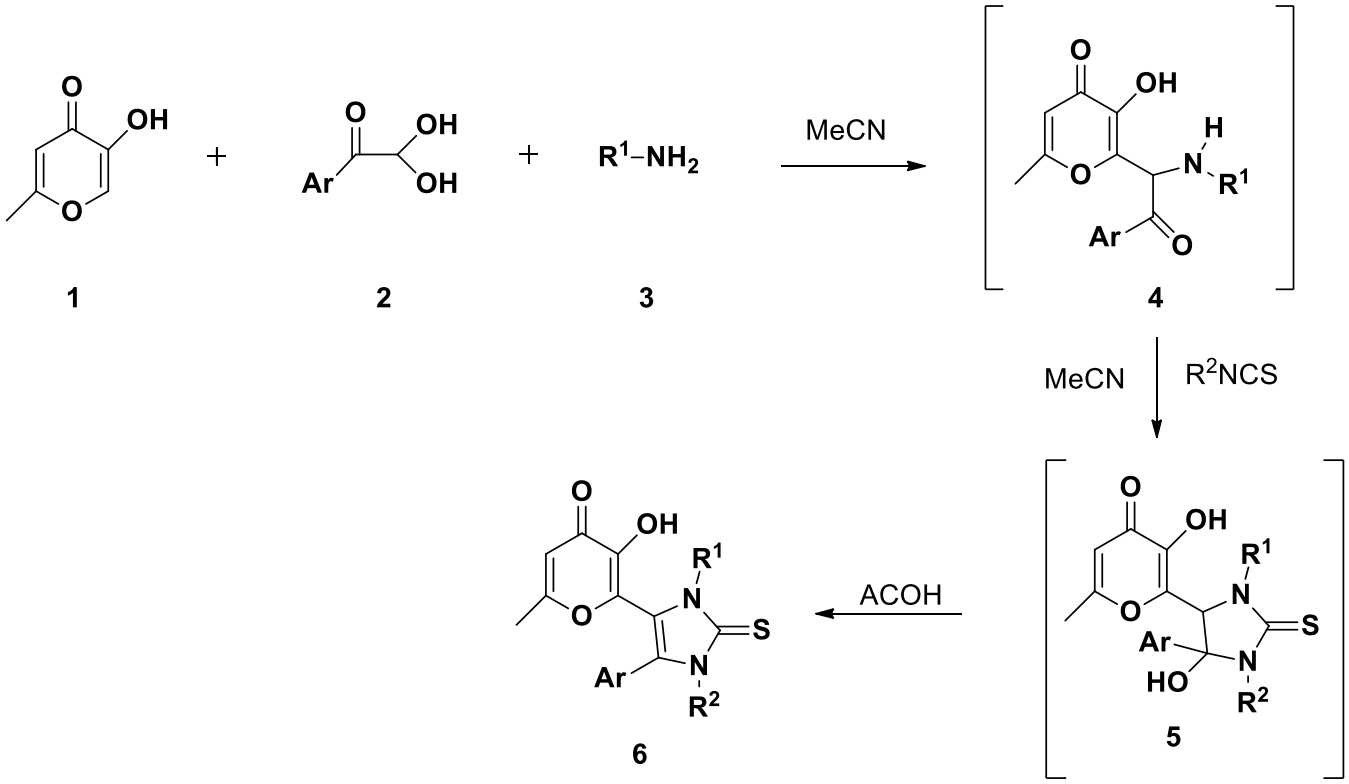
antitumor[7], CNS-active[8], analgesic[9], antimicrobial [10], and chemotherapy[11]. Isoxazoles displayes a wide range of organic reactivities and could be used as an affective means of preparing new molecular scaffolds [12] .

In view of the potential bioactivity of isoxazole derivatives and in continuation of our work on the effective preparative methods for the synthesis of various polyheterocyclic systems[13-16]. we undertook the synthesis of present work. In the present paper, we adopted a convenient one-pot approach for the synthesis of substituted imidazole-2-thiones containing isoxazole and allomaltol fragments. This method is based on the multi-component reaction of allomaltol, arylglyoxals, isoxazole amines, followed by interaction with substituted isothionates .

The general approaches for the synthesis of imidazole-2-thiones is based on the reaction of α-amino ketones with isothiocyanates [17-19]. One of the starting material i.e., α-amino ketones have low stability, therefore for the preparation of these compounds *in situ* generation is most appropriate, Keeping this in to consideration, in this synthetic protocol, we generated α-amino ketones *in situ*, then reacted with isothiocyanates to obtain the desired products *viz*., imidazole-2-thiones.



Scheme-1 One pot strategy for the synthesis of 3-hydroxy-6-methyl-2-(1-methyl-3-(5-methylisoxazol-3-yl)-5-aryl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-4*H*-pyran-4-ones

Compound	Ar	R^1	R^2
6a	C_6H_5	5-methyl-3-isoxazolyl	CH_3
6b	4-$OCH_3C_6H_4$	5-methyl-3-isoxazolyl	C_6H_5
6c	4-ClC_6H_4	5-methyl-3-isoxazolyl	4-$OCH_3C_6H_4$
6d	3-$OCH_3C_6H_4$	5-methyl-3-isoxazolyl	4-ClC_6H_4
6e	C_6H_5	3-methyl-5-isoxazolyl	CH_3
6f	4-$OCH_3C_6H_4$	3-methyl-5-isoxazolyl	C_6H_5
6g	4-ClC_6H_4	3-methyl-5-isoxazolyl	4-$OCH_3C_6H_4$

6h	3-$OCH_3C_6H_4$	3-methyl-5-isoxazolyl	4-ClC_6H_4
6i	C_6H_5	3-methyl-5-styryl-4-isoxazolyl	CH_3
6j	4-$OCH_3C_6H_4$	3-methyl-5-styryl-4-isoxazolyl	C_6H_5
6k	4-ClC_6H_4	3-methyl-5-styryl-4-isoxazolyl	4-$OCH_3C_6H_4$
6l	3-$OCH_3C_6H_4$	3-methyl-5-styryl-4-isoxazolyl	4-ClC_6H_4

The raction of allomaltol **1**, aryl glyoxal **2** and different isoxazole amines **3** under refluxing conditions in CH_3CN solvent produced α-amino ketones **4** which were not isolated, Further more, the addition of isothiocyanates to the reaction mixture leads to the formation of substituted imidazolidine -2-thione **5** *in situ*, which was then dehydrated by addition of acetic acid to afford the target compounds *viz*., imidazole-2-thiones.**6.**

The prominent feature of the present investigation is the employment of acetonitrile as a solvent for generation of α-amino ketones **4** *in situ*, and it also helps to produce imidazolidine -2-thiones **5** up on interaction with isothiocyanates. It is observed that acetic acid is necessary for acid-catalysed dehydration for the conversion of imidazolidine-2-thiones **5** in to imidazole-2-thiones **6**. The most advantages of this ptotocol involving one-pot method affords the title compounds **6** in good yields, compared to the standard three-step procedure due to circumventing the isolation of the intermediates **4** and **5**. Taking this in to account the present methodology significantly more appreciate to produce wide range of hydroxyl containing terarylenes with an imidazole -2-thione bridge fragment carrying isoxazole fragment.

This reaction was initially conducted by employing different solvents such as CH_2Cl_2, THF, toluene, EtOAc and dioxane. In all these cases the product yields varied between 40-50%. The better results were obtained with CH_3CN solvent under reflux condition which produced 85% yield. When the same reaction was carried out with CH_3CN at room temperature the product yield was between 50-55%. Refluxing conditions required 1 hr for better yields. Either by increasing the refluxing period no positive result was obtained.

Table 1 optimization of reaction conditions [a]

Entry	Solvent	Time, h	Temp, ^0C	Yield (%)
1	CH_2Cl_2	1	reflux	45
2	THF	1	reflux	60
3	Toluene	1	reflux	50
4	EtOAc	1	reflux	40
5	Dioxane	1	reflux	65
6	CH_3CN	1	reflux	85
7	CH_3CN	1	r.t	50
8	CH_3CN	4	reflux	80

[a] A mixture of **1** (1 mmol), **2** (1 mmol), **3** (1 mmol), reflux in CH_3CN, followed by heating with ACOH

Experimental Section

Melting points have been determined on a Cintex melting point apparatus. TLC has been performed on Merck precoated 60 F_{254} silica gel plates. Visualization is done by exposing to iodine vapour. IR spectra (KBr pellet) have been recorded on a Perkin- Elmer BX series FT-IR spectrometer. ^1H NMR spectra are recorded on a Bruker 300 MHz spectrometer. ^{13}C NMR spectra are recorded on a Bruker 75 MHz spectrometer. Chemical shift values are given in δ ppm with tetramethyl silane as an internal standard. ESI -MS spectra are recorded on a Agilent LC-MSD mass spectrometer. Elemental analyses are performed on a Carlo Erba 106 and Perkin-Elmer model 240 analyzers.

General procedure for the synthesis of 3-hydroxy-6-methyl-2-(1-methyl-3-(5-methylisoxazol-3-yl)-5-phenyl-2-thioxo-2,3-dihydro-1H-imidazol-4-yl)-4H-pyran-4-one (6a-l)

A mixture of allomaltol **1** (1 mmol), arylglyoxal **2** (1 mmol), and isoxazole amine **3** (1 mmol) was taken in CH_3CN solvent (10 ml) and the contents are stirred at room temperature for 15 min. Later substituted isothiocyanates **4** (2 mmol) was added and the reaction mixture was refluxed for 1 h. After completion of the reaction (monitored by TLC), the solution was evaporated in vacuum. To the residue acetic acid (10 ml) was added and it was refluxed for another 1 h. After the formation of the desired product, as indicated by TLC, the reaction mixture was evaporated in vacuum and the resulting solid was recrystallized from ethanol to get the pure product **6**.

3-Hydroxy-6-methyl-2-(1-methyl-3-(5-methylisoxazol-3-yl)-5-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-4*H*-pyran-4-one (6a). Pale Yellow solid, m.p. 140-42°C; IR (KBr, cm^{-1}): ν_{max}: 3400 (OH), 1710 (C=O), 1190 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.24 (s, 3H, isoxazole-CH_3), 2.36 (s, 3H, CH_3), 3.07 (s, 3H, N-CH_3), 6.03 (s, 1H, isoxazole-H), 6.56 (s, 1H), 6.96-7.09 (m, 5H, Ar-H), 12.44 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.45, 21.86, 39.65, 113.25, 118.69, 120.25, 121.36, 126.25, 127.69, 128.35, 129.87, 130.35, 135.25, 141.35, 149.68, 151.24, 168.35, 166.38, 181.92, 192.35. ESI-MS: *m/z* 396 $[M + H]^+$. Anal. Calcd. for $C_{20}H_{17}N_3O_4S$: C, 60.73; H, 4.34; N, 10.65. Found: C, 60.75; H, 4.33; N, 10.63%.

3-Hydroxy-2-(5-(4-methoxyphenyl)-3-(5-methylisoxazol-3-yl)-1-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-6-methyl-4*H*-pyran-4-one (6b). Pale Yellow solid, m.p. 148-50°C; IR (KBr, cm^{-1}): ν_{max}: 3410 (OH), 1715 (C=O), 1196 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.22 (s, 3H, isoxazole-CH_3), 2.34 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.05 (s, 1H), 6.62 (s, 1H, isoxazole ring-H), 6.88-7.50 (m, 9H, Ar-H), 12.48 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.69, 22.26, 54.68, 114.05, 116.35, 117.89, 117.32, 119.63, 121.15, 122.16,123.65, 125.32, 126.81, 127.07, 127.98, 128.69, 129.55, 131.25, 136.20, 142.25, 150.36, 152.64, 165.25, 166.23, 180.92, 191.69. ESI-MS: *m/z* 488 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{21}N_3O_5S$: C, 64.09; H, 4.34; N, 8.60. Found: C, 64.06; H, 4.31; N, 8.62%.

2-(5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(5-methylisoxazol-3-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one l (6c). Pale Yellow solid, m.p. 156-58°C; IR (KBr, cm^{-1}): ν_{max}: 3415 (OH), 1712 (C=O), 1190 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.20 (s, 3H, isoxazole-H), 2.30 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.08 (s, 1H), 6.65 (s, 1H, isoxazole ring- CH_3), 6.92-7.56 (m, 8H, Ar-H), 12.40 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.72, 23.16, 55.53, 113.95, 115.25, 116.39, 117.22, 118.73, 120.35, 121.96, 122.86, 124.52, 125.88, 126.37, 127.92, 128.25, 129.32, 130.65, 134.50, 141.65, 148.96, 153.84, 164.75, 165.39, 179.22, 190.29. ESI-MS: *m/z* 522 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{20}ClN_3O_5S$: C, 59.84; H, 3.80; N, 8.03;. Found: C, 59.86; H, 3.83; N, 8.02%.

2-(1-(4-Chlorophenyl)-5-(3-methoxyphenyl)-3-(5-methylisoxazol-3-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one (6d). Pale Yellow solid; m.p. 165-67°C; IR (KBr, cm^{-1}): ν_{max}: 3417 (OH), 1708 (C=O), 1195 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.23 (s, 3H, isoxazole- CH_3), 2.34 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.10 (s, 1H), 6.63 (s, 1H, isoxazole ring-H), 6.88-7.50 (m, 8H, Ar-H), 12.44 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 13.12, 22.86, 56.23, 112.65, 114.85, 115.55, 117.01, 118.68, 119.39, 120.88, 123.92, 124.32, 125.36, 126.30, 127.96, 128.21, 129.65, 132.25, 135.73, 144.05, 147.66, 155.24, 162.70, 165.55, 180.12, 191.09. ESI-MS: *m/z* 522 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{20}ClN_3O_5S$: C, 59.84; H, 3.80; N, 8.03;. Found: C, 59.88; H, 3.82; N, 8.06%..

3-Hydroxy-6-methyl-2-(1-methyl-3-(3-methylisoxazol-5-yl)-5-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-4*H*-pyran-4-one (6e). Pale Yellow solid, m.p. 174-76°C; IR (KBr, cm^{-1}): ν_{max}: 3415 (OH), 1715 (C=O), 1190 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.20 (s, 3H, isoxazole- CH_3), 2.35 (s, 3H, CH_3), 3.08 (s, 3H, N-CH_3), 6.15 (s, 1H), 6.66 (s, 1H, isoxazole ring-H), 6.92-7.55 (m, 5H, Ar-H), 12.40 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.95, 21.39, 40.25, 100.35, 113.88, 119.25 125.88, 126.24, 127.84, 128.75, 129.21, 134.25, 139.87,

145.27, 150.32, 159.78, 168.97, 170.52, 180.72, 190.35;. ESI-MS: *m/z* 396 $[M + H]^+$. Anal. Calcd. for $C_{20}H_{17}N_3O_4S$: C, 60.72,; H, 4.33; N, 10.66;. Found: C, 60.75,; H, 4.30; N, 10.63%.

3-Hydroxy-2-(5-(4-methoxyphenyl)-3-(3-methylisoxazol-5-yl)-1-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-6-methyl-4*H*-pyran-4-one (6f). Pale Yellow solid, m.p. 179-81°C; IR (KBr, cm^{-1}): ν_{max}: 3412 (OH), 1710 (C=O), 1193 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.22 (s, 3H, isoxazole- CH_3), 2.31 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.12 (s, 1H), 6.70 (s, 1H, isoxazole ring-H), 6.75-7.35 (m, 9H, Ar-H), 12.45 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 13.35, 22.69, 56.25, 101.25, 114.38, 116.87, 118.41, 120.36, 121.54, 122.30, 126.80, 127.44, 128.14, 129.44, 130.14, 133.20, 140.37, 144.77, 151.34, 160.28, 169.90, 171.02, 179.82, 189.65;. ESI-MS: *m/z* 488 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{21}N_3O_5S$: C, 64.02; H, 4.30; N, 8.60;. Found: C,, 64.05; H, 4.34; N, 8.62%.

2-(5-(4-Chlorophenyl)-1-(2-methoxyphenyl)-3-(3-methylisoxazol-5-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one (6g). Pale Yelllow solid, m.p. 185-87°C; IR (KBr, cm^{-1}): ν_{max}: 3410 (OH), 1715 (C=O), 1196 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.25 (s, 3H, isoxazole- CH_3), 2.33 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.14 (s, 1H), 6.69 (s,1H, isoxazole ring-H), 6.85-7.45 (m, 8H, Ar-H), 12.40 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 14.45, 20.79, 57.55, 102.20, 115.38, 117.87, 119.55, 121.66, 122.94, 123.60, 125.82, 127.65, 128.34, 129.64, 130.21, 131.02, 131.84, 134.60, 141.67, 145.78, 150.33, 161.69, 168.80, 172.92, 180.80, 190.05;. ESI-MS: *m/z* 522 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{20}ClN_3O_5S$: C, 59.85; H, 3.86; N, 8.03. Found: C, 59.88; H, 3.83; N, 8.06;%.

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2-(1-(4-Chlorophenyl)-5-(3-methoxyphenyl)-3-(3-methylisoxazol-5-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one (6h). Pale Yellow solid, m.p. 193-95°C; IR (KBr, cm^{-1}): ν_{max}: 3415 (OH), 1710 (C=O), 1192 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.22 (s, 3H, isoxazole-H), 2.35 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.17 (s, 1H), 6.63 (s, 1H, isoxazole ring-H), 6.80-7.55 (m, 8H, Ar-H), 12.45 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 13.25, 21.99, 58.25, 101.00, 116.32, 117.65, 118.37, 119.55, 120.63, 121.94, 122.30, 126.32, 127.15, 129.34, 130.24, 131.15, 132.89, 135.63, 142.68, 146.25, 151.23, 162.72, 169.83, 173.90, 179.30, 189.25;. ESI-MS: *m/z* 522 $[M + H]^+$. Anal. Calcd. for $C_{26}H_{20}ClN_3O_5S$: C, 59.84; H, 3.80; N, 8.03.; Found: C, 59.88; H, 3.83; N, 8.02;%.

(E)-3-Hydroxy-6-methyl-2-(1-methyl-3-(3-methyl-5-styrylisoxazol-4-yl)-5-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-4*H*-pyran-4-one (6i). Pale Yellow solid, m.p. 199-201°C; IR (KBr, cm^{-1}): ν_{max} 3412 (OH), 1713 (C=O), 1190 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.24 (s, 3H, isoxazole- CH_3), 2.36 (s, 3H, CH_3), 3.08 (s, 3H, N-CH_3), 6.20 (s, 1H), 6.92 (s, 1H, CH=CH), 6.98 (s, 1H, CH=CH), 6.70-7.65 (m, 10H, Ar-H), 12.40 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.54, 22.36, 39.85, 100.30, 110.47, 113.68, 117.65, 120.27, 122.91, 124.65, 125.68, 126.31, 127.57, 129.24, 130.25, 132.57, 133.01, 134.87, 135.45, 137.69, 139.25, 141.35, 148.36, 150.67, 157.24, 168.34, 182.45, 190.22.;. ESI-MS: *m/z* 498 $[M + H]^+$. Anal. Calcd. for $C_{28}H_{23}N_3O_4S$: C, 67.63; H, 4.60; N, 8.48. Found: C, 67.60; H, 4.62; N, 8.45;%.

(E)-3-Hydroxy-2-(5-(4-methoxyphenyl)-3-(3-methyl-5-styrylisoxazol-4-yl)-1-phenyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-6-methyl-4*H*-pyran-4-one (6j). Pale Yellow solid,, m.p. 205-07°C; IR (KBr, cm^{-1}): ν_{max} 3415 (OH), 1718 (C=O), 1195 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.23 (s, 3H, isoxazole- CH_3), 2.34 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.24 (s, 1H), 6.90 (s, 1H, CH=CH), 6.95 (s, 1H, CH=CH), 6.75-7.62 (m, 14H, Ar-H), 12.45 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 13.54, 22.36, 55.85, 100.30, 110.47, 112.65, 113.02, 113.68, 117.65, 120.27, 122.91, 124.65, 125.68, 126.31, 127.57, 129.24, 130.25, 131.44, 132.57, 133.01, 134.87, 135.45, 136.01, 137.69, 138.24, 139.25,140.01, 141.35, 148.36, 150.67, 157.24, 168.34, 182.45, 190.22.;. ESI-MS: *m/z* 590 $[M+H]^+$. Anal. Calcd. for $C_{34}H_{27}N_3O_5S$: C, 69.24; H, 4.55; N, 7.16. Found: C, 69.26; H, 4.58; N, 7.13;%.

(E)-2-(5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(3-methyl-5-styrylisoxazol-4-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one (6k)

Pale Yellow solid,, m.p. 216-18°C; IR (KBr, cm^{-1}): ν_{max} 3415 (OH), 1718 (C=O), 1195 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.23 (s, 3H, isoxazole- CH_3), 2.34 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.24 (s, 1H), 6.90 (s, 1H, CH=CH), 6.93 (s, 1H, CH=CH), 6.70-7.65 (m, 13H, Ar-H), 12.48 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 12.54, 21.16, 56.25, 101.20, 111.27, 113.15, 114.02, 114.98, 116.60, 121.01, 122.41, 123.61, 124.87, 125.11, 127.52, 128.98, 131.35, 132.46, 133.50, 134.06, 135.55, 136.45, 135.11, 136.88, 137.21, 140.21,141.21, 142.30, 147.16, 151.60, 158.21, 167.31, 180.36, 189.20.;. ESI-MS: *m/z* 624 $[M+H]^+$. Anal. Calcd. for $C_{34}H_{26}ClN_3O_5S$: C, 65.45; H, 4.19; N, 6.71. Found: C, 65.48; H, 4.17; N, 6.74;%.

(E)-2-(1-(4-Chlorophenyl)-5-(3-methoxyphenyl)-3-(3-methyl-5-styrylisoxazol-4-yl)-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)-3-hydroxy-6-methyl-4*H*-pyran-4-one (6l)

Pale Yellow solid,, m.p. 222-24°C; IR (KBr, cm^{-1}): ν_{max} 3412 (OH), 1714 (C=O), 1193 (C=S); ^{1}H NMR (300 MHz, $CDCl_3$): δ: 2.21 (s, 3H, isoxazole- CH_3), 2.32 (s, 3H, CH_3), 3.68 (s, 3H, Ar-OCH_3), 6.21 (s, 1H), 6.89 (s, 1H, CH=CH), 6.90 (s, 1H, CH=CH), 6.74-7.55 (m, 13H, Ar-H), 12.45 (s, 1H, Ar-OH, D_2O exchangeable); ^{13}C NMR (75MHz, $CDCl_3$): δ: 13.24, 22.10, 55.85, 100.89, 112.22, 114.15, 114.69, 115.18, 117.67, 120.31, 121.36, 122.62, 123.25, 124.32, 126.72, 127.98, 130.69, 133.42, 134.69, 135.26, 136.53, 137.42, 138.01, 139.00, 140.08, 141.36,142.31, 144.00, 146.98, 150.67, 159.22, 168.25, 179.24, 190.02.; ESI-MS: *m/z* 624 $[M+H]^+$. Anal. Calcd. for $C_{34}H_{26}ClN_3O_5S$: C, 65.49; H, 4.15; N, 6.76. Found: C, 65.48; H, 4.17; N, 6.74;%.

Conclusion

In conclusión, a novel eficient one-pot protocol was developed for the synthesis of imidazole-2-thiones carrying allomaltol and isoxazole fragments. It has been demonstrated that the key intermédiate of the process are substituted α-aminoketones and imidazolidine -2-thiones, which were not isolated, and only the final target compounds were purified. The synthesis is efficient, generating a convenient access to the hydroxy containing terarylenes. The advantages of present protocol includes mild conditions, atom economy, easy work- up procedure, without intervention of tedious chromatographic process and affording good yields.

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